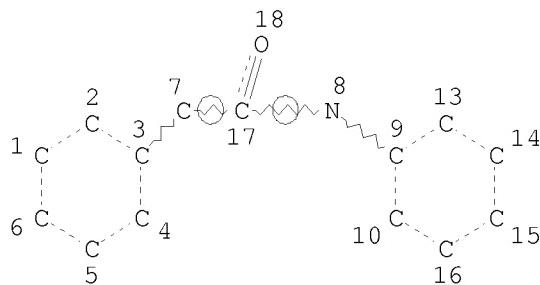


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=> d 11  
L1 HAS NO ANSWERS  
L1 STR
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NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

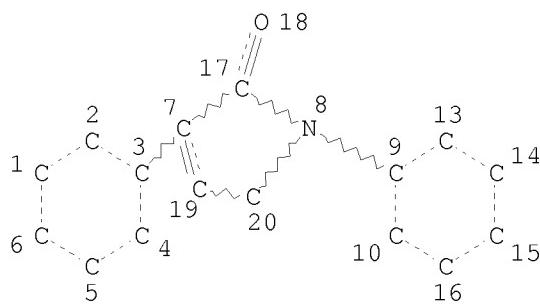
GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

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=> d his 13
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(FILE 'REGISTRY' ENTERED AT 09:27:52 ON 26 FEB 2008)  
L3 8571 S L1 FUL
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=> d 116  
L16 HAS NO ANSWERS  
L16 STR
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NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

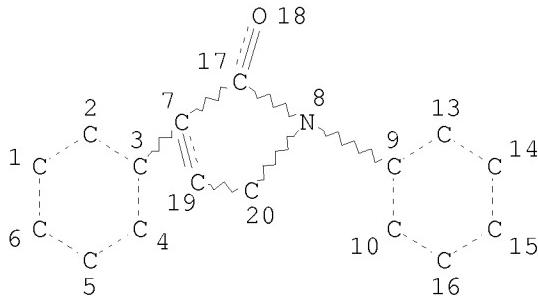
GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

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=> d his 117
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(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)  
L17 984 SEARCH L16 SSS SUB=L3 FUL

=> d 118  
L18 HAS NO ANSWERS  
L18 STR



NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RSPEC 7  
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> d his 119

(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)  
L19 908 SEARCH L18 SSS SUB=L3 FUL

=> d his 120-128

(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)  
L20 328 S L19 AND (PYRROL?(L)DIONE)  
L21 580 S L19 NOT L20  
L22 125 S L21 AND (DIOXO? OR DIKETO?)  
L23 455 S L21 NOT L22

FILE 'CAPLUS' ENTERED AT 09:55:59 ON 26 FEB 2008  
L24 62 S L23  
L25 4 S L24 AND (DEPRES? OR ANXI? OR CNS)  
L26 58 S L24 NOT L25  
L27 50 S L26 AND PY<=2002  
L28 21 S L27 AND P/DT

=> d bib abs 125 1-4

L25 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:625334 CAPLUS  
DN 145:271603  
TI Diaryl substituted pyrrolidinones and pyrrolones as 5-HT2C inhibitors:  
Synthesis and biological evaluation  
AU Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna; Hamprecht,  
Dieter; Bonanomi, Giorgio; Checchia, Anna; Jaxa-Chamiec, Albert; Damiani,  
Federica; Davalli, Silvia; Donati, Daniele; Gallotti, Chiara; Petrone,  
Marcella; Rinaldi, Marilisa; Riley, Graham; Terreni, Silvia; Wood, Martyn

CS GlaxoSmithKline Psychiatry Centre of Excellence for Drug Discovery,  
Verona, 4, 37135, Italy  
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(15), 3906-3912  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier B.V.  
DT Journal  
LA English  
AB Within the continuous quest for the discovery of novel compds. able to treat anxiety and depression, the generation of a pharmacophore model for 5-HT2C receptor antagonists and the discovery of a new class of potent and selective 5-HT2C mols. are reported.  
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:1019875 CAPLUS  
DN 141:406136  
TI Compositions of a cyclooxygenase-2 selective inhibitor and a peroxisome proliferator activated receptor agonist for the treatment of ischemia-mediated central nervous system disorders  
IN Needleman, Philip; Obukowicz, Mark G.; Arneric, Stephen P.  
PA Pharmacia Corporation, USA  
SO PCT Int. Appl., 164 pp.  
CODEN: PIXXD2  
DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004100895	A2	20041125	WO 2004-US14741	20040512
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005107387	A1	20050519	US 2004-844269	20040512
PRAI	US 2003-470240P	P	20030513		

OS MARPAT 141:406136  
AB The invention provides compns. and methods for the treatment of ischemia-mediated central nervous system disorders. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemia-mediated disorder comprising the administration to a subject of a peroxisome proliferator activated receptor agonist in combination with a cyclooxygenase-2 selective inhibitor.

L25 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:756686 CAPLUS  
DN 141:277494  
TI Preparation of diaryl substituted pyrrolidinones and pyrrolones having activity at 5-HT2c receptor  
IN Damiani, Federica; Hamprecht, Dieter; Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna  
PA Glaxo Group Limited, UK  
SO PCT Int. Appl., 32 pp.

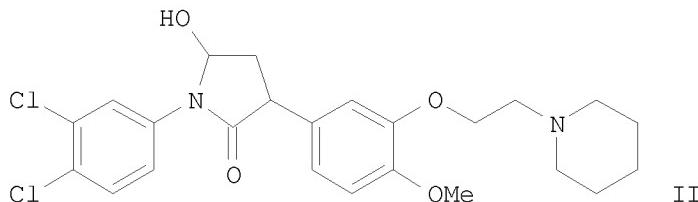
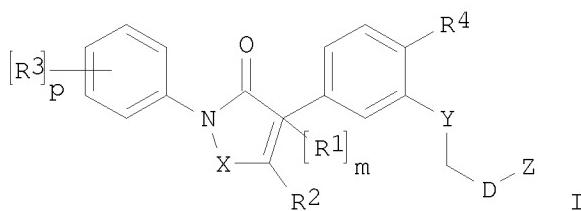
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004078718	A1	20040916	WO 2004-EP1843	20040224
	WO 2004078718	A8	20050526		
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	EP 1599445	A1	20051130	EP 2004-713874	20040224
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006519241	T	20060824	JP 2006-504465	20040224
	US 2006205788	A1	20060914	US 2006-548118	20060518
PRAI	GB 2003-5024	A	20030305		
	WO 2004-EP1843	W	20040224		
OS	MARPAT 141:277494				
GI					

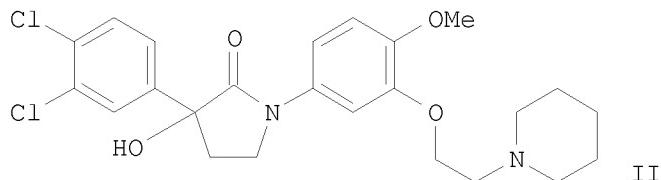
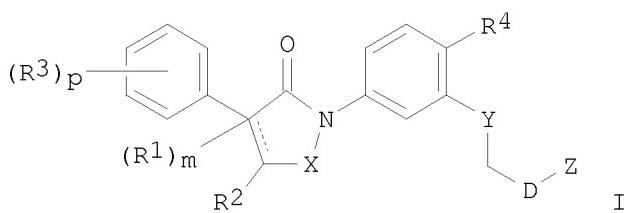


AB The title compds. [I; R1 = H, F, Cl, OH, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0-1; R2 = H, halo, CN, NO<sub>2</sub>, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; X = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, (CH<sub>2</sub>)<sub>3</sub>, C(CH<sub>3</sub>)<sub>2</sub>, CH:CHCH<sub>2</sub>, CH<sub>2</sub>CH:CH or CHR<sub>5</sub> (wherein R<sub>5</sub> = H, halo, OH, CN, NO<sub>2</sub>, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio); R<sub>3</sub> = halo, CN, alkyl, cycloalkyl, cycloalkyloxy, alkoxy, alkylthio, OH, NH<sub>2</sub>, mono- or dialkylamino, etc.; p = 0-3; R<sub>4</sub> = H, halo, OH, CN, NO<sub>2</sub>, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; Y = O, S, CH<sub>2</sub> or NR<sub>10</sub> (wherein R<sub>10</sub> = H, alkyl); D = a single bond, CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub> or CH:CH; Z = NR<sub>11</sub>R<sub>12</sub> (where R<sub>11</sub> and R<sub>12</sub> = H, alkyl, (un)substituted N-linked or C-linked 4-7 membered

heterocyclic group)] and their pharmaceutically acceptable salts, useful in treating, for example, depression and anxiety, were prepared. E.g., a multi-step synthesis of II, was given. All exemplified compds. I were tested for their affinity for the 5-HT2c receptor, and were found to have pKi values >5.8. The pharmaceutical composition comprising the compound I is disclosed.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25	ANSWER 4 OF 4	CAPLUS	COPYRIGHT 2008 ACS on STN
AN	2003:855908	CAPLUS	
DN	139:350638		
TI	3-Aryl-1-[4-alkoxy-3-[2-(piperidin-1-yl)ethoxy]phenyl]pyrrolidin-2-ones and analogs with affinity at 5-HT2C receptors, and use thereof in therapy, particularly as antidepressants and anxiolytics, and their preparation and pharmaceutical compositions		
IN	Damiani, Federica; Hamprecht, Dieter; Jaxa-Chamiec, Albert Andrzej; Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna		
PA	Glaxo Group Limited, UK		
SO	PCT Int. Appl., 74 pp. CODEN: PIXXD2		
DT	Patent		
LA	English		
FAN.CNT 1			
PATENT NO.	KIND	DATE	APPLICATION NO.
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PI WO 2003089409	A1	20031030	WO 2003-EP4180 20030417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003222832	A1	20031103	AU 2003-222832 20030417
EP 1497265	A1	20050119	EP 2003-718783 20030417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005529117	T	20050929	JP 2003-586130 20030417
US 2005203079	A1	20050915	US 2005-511769 20050502
PRAI GB 2002-9029	A	20020419	
GB 2002-20781	A	20020906	
WO 2003-EP4180	W	20030417	
OS MARPAT 139:350638			
GI			



AB Title compds. I and their pharmaceutically acceptable salts are disclosed [wherein: R<sub>1</sub> = H, OH, F, Cl, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0 or 1; R<sub>2</sub> = H, halo, cyano, NO<sub>2</sub>, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-C<sub>1</sub>-6alkylamino, or N-linked 4-7 membered heterocyclic; X = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, (CH<sub>2</sub>)<sub>3</sub>, CH:CHCH<sub>2</sub>, CH<sub>2</sub>CH:CH, or CHR<sub>5</sub>; R<sub>3</sub> = halo, cyano, alkyl, cycloalkyl, cycloalkyloxy, Cl-alkoxy, Cl-6alkylthio, OH, amino, mono- or di-C<sub>1</sub>-6alkylamino, N-linked 4-7 membered heterocyclic, NO<sub>2</sub>, haloalkyl, haloalkoxy, aryl, arylalkyl, arylalkyloxy, arylalkylthio, COOR<sub>6</sub>, CONR<sub>7</sub>R<sub>8</sub>, or COR<sub>9</sub>; R<sub>4</sub> = H, halo, OH, cyano, NO<sub>2</sub>, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-alkylamino or N-linked 4-7 membered heterocyclic; R<sub>5</sub> = H, halo, OH, cyano, NO<sub>2</sub>, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio; R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, and R<sub>9</sub> = H or alkyl; p = 0, 1, 2, or 3; Y = O, S, CH<sub>2</sub>, or NR<sub>10</sub>; R<sub>10</sub> = H or alkyl; D = bond, CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub>, or CH:CH; Z = (un)substituted C-linked 4-7 membered heterocyclic, or Z = NR<sub>11</sub>R<sub>12</sub>; R<sub>11</sub> and R<sub>12</sub> = H or alkyl]. Methods of preparation and uses of I in therapy, particularly for treating CNS disorders such as depression and anxiety, are also disclosed. The affinities of compds. I for 5-HT<sub>2C</sub> receptors were determined by assessing their ability to displace [<sup>3</sup>H]-mesulergine from rat or human 5-HT<sub>2C</sub> clones expressed in 293 cells in vitro, as described in WO 94/04533. All example compds. were so tested and had pKi values >5.8. Some compds. I show a considerably higher affinity, in the range of 7.0 to >9.0 in human cells. Approx. 45 synthetic examples and approx. 75 precursor preps. are given. For instance, 3,4-dichlorophenylacetic acid underwent a sequence of (1)  $\alpha$ -lithiation and allylation, (2) amidation with 2-(5-amino-2-methoxyphenoxy)ethyl acetate, (3) OsO<sub>4</sub>-catalyzed glycolation of the alkene, and periodate oxidation of the glycol with cyclic hemiaminal formation, to give a 5-hydroxy-2-pyrrolidinone derivative, (4) reduction of the latter to remove 5-hydroxy, (5) saponification of the acetate ester sidechain to an alc., (6) conversion of the alc. to a mesylate ester, and (7) aminolysis of the mesylate with piperidine in the presence of K<sub>2</sub>CO<sub>3</sub> and NaI, followed by benzylic hydroxylation with air over 18 h, to give title compound II.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT